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Context and Pain Perception: Stress Induced Analgesia as a Function of Similarity in Odor and Apparatus Cues between Stress and Analgesia Assessment Environments

by

Desmond J. Coen

(C)

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES AND RESEARCH

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE

OF Master of Science

Department of Psychology

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FACULTY OF GRADUATE STUDIES AND RESEARCH

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research, for acceptance, a thesis entitled Context and Pain Perception: Stress Induced Analgesia as a Function of Similarity in Odor and Apparatus Cues between Stress and Analgesia Assessment Environments submitted by Desmond J. Coen in partial fulfilment of the requirements for the degree of Master of Science.

[redacted]

Date. December 20, 1984

Abstract

Two experimnents were conducted to assess the role of contextual stimuli in the development of stress induced analgesia (SIA) in rats. Experiment 1 manipulated two contextual odors factorially between tail shock and later tail flick analgesia assessment environments to determine if maximal SIA depended upon a similarity of odor conditions. Odor conditions did not influence the magnitude of SIA. An unpredicted long term SIA effect was observed in experiment 1. Experiment 2 was conducted to determine the time course of this long term effect and determine if apparatus cues were responsible for this finding. Apparatus cues were found responsible for the persistance of the SIA. The implications of these results for current research in aversively motivated behaviors were discused in detail. Specifically the relevance of these findings for the learned helplessness model of Maier and Seligman(1976) and the Maier(1979, 1983) "controllability" explanation of SIA were discussed. Both of these explanations fail to predict the results of the present study. Similarity between stress and test environments is suggested to be the prepotent variable in determining the magnitude and time course of SIA. A brief review of literature covering context and aversively motivated behavior was included to suggest ways more potent and long lasting SIA than previously demonstrated can be achieved by applying principles of classical and instrumental conditioning.

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I. Introduction

The purpose of this study was to examine the effect of changes in environmental context upon the magnitude and time course of stress induced analgesia (SIA). The main thesis was that a high degree of similarity must exist between the analgesia measurement context and the context in which the analgesia inducing stressor was originally administered if maximal SIA is to be observed. Identifying the critical environmental parameters that influence endogenous pain control systems is important for two reasons. First isolating the critical variables will provide a fuller understanding of the operating characteristics of endogenous pain control systems in particular, and of habituation to noxious stimuli in general. Second, techniques developed herein, which selectively amplify or inhibit responses to noxious stimulation, will be useful in developing clinical tools that allow less reliance on more invasive and traditional forms of pain control (e.g. surgical blocks, drug treatment, counterirritation).

Studies examining endogenous pain control systems have only recently begun to assess the role of environmental factors in the SIA paradigm. For example, Hayes, Bennett, Newlon and Mayer(1978) and Hayes, Price, Bennett, Wilcox and Mayer(1978) found that rats learned to associate environmental cues with footshock. In these studies the shock grid chambers served as the conditioned stimulus (CS), foot shock was the unconditioned stimulus (UCS), and SIA was

the unconditioned response (UCR). CS-UCS pairings eventually produced analgesia elicited by the non-electrified grid chamber. Oliverio and Castellano(1982) confirmed these findings by conditioning analgesia to a tone stimulus. More recent studies have attempted to isolate the neural circuitry subsuming classically conditioned SIA. Watkins, Cobelli, Newsome and Mayer(1982) ruled out pituitary and adrenal opiate activity in a lesion study and concluded that the phenomena was mediated by neural rather than hormonal factors.

The present study was designed to extend the above findings by more precisely manipulating context. Specifically the role of odor as a contextual cue was considered. Most SIA studies employ rats as subjects. The laboratory rat has a very keen sense of smell and a disproportionate amount of the rat brain (in comparison to the average human brain) is devoted to olfactory activity. Thus it is pertinent to consider whether or not odors could serve as salient cues to which rats would be particularly responsive. This possibility is especially interesting because rats introduce odor cues into experimental situations themselves (through urination, defecation, perspiration). Thus the possibility exists that a class of contextual stimuli exists which are at least as salient as the CSs normally employed by experimenters (e.g. tone CSs, apparatus cues). Most important, however, this class of stimuli has been ignored in SIA studies to date despite

experimental evidence that supports the suggestion that it may be worthwhile to consider the salience of odor cues in SIA studies.

Pierson(1974) demonstrated that rats are capable of discriminating between similar odors in a conditioned suppression procedure. Valenta and Rigby(1968) and also Mackay and Sim-Laing(1980) noted that rats could discriminate between the odors of stressed or unstressed rats (even though they could not distinguish the odors of individual rats). King and Pfister(1975) found that unstressed rats preferred to spend time in the presence of odors from stressed rats while the stressed rats avoided the odor of stressed conspecifics. King(1969) found that rats were more succeptible to odors than visual cues in a simple fear conditioning task. Smith and Spear(1978) and Rudy and Cheattle(1978) confirmed this finding in studies looking at two different types of learning in neonatal rats. These neonatal studies testified to the salience of odor cues by demonstrating that associative learning occurred in rats at an age much lower than previously thought possible. Clearly odor can act as a CS in aversive conditioning and may be introduced into stress situations by the rats themselves.

Recent support for the salience of odors in mediating responses to stress was provided by Minor and LoLordo(1984), who examined the effects of contextual odor upon escape learning in rats previously exposed to inescapeable shock (80 five second 1.0 mA shocks). They found that inescapable

shock was detrimental to later escape learning only when the shock and later escape-avoidance learning environments were scented with the same odor. This finding is quite striking because it conflicts with a large body of literature that examines the effects of the type of uncontrollable stress used by Minor and LoLordo(1984). The learned helplessness model in particular (Overmeir and Seligman, 1967; Seligman and Beagley, 1975; Maier and Seligman, 1976) has been a very popular explanation of performance deficits following uncontrollable stress.

The broad literature that supports this model has tended to support the notion that the physical effects of stress itself are not critical in determining later performance deficits, but rather the absence of control over the stress or a lack of contingency between an animal's responses and termination of stress appears to be the important variable. The learned helplessness model explicitly excludes contextual factors in favour of a cognitive explanation of learned helplessness (Seligman and Beagley, 1975).

The type of odor control measures that Minor and LoLordo suggest are necessary are not employed in this literature. The absence of these control measures may be problematic since most experimenters do not remove odors from experimental apparatus between the testing of each animal. Typically, experimental equipment is contaminated with the odors of other animals that have been stressed in

the same apparatus. The cleaning procedures that are employed are rarely reported, or, if reported, are not thorough enough to remove the powerful scents left behind by stressed animals. Thus it is possible that many learned helplessness experiments have been confounded by the effects of odors acting as effective danger signals. That is, signals which have preceded uncontrollable aversive stimulation in previous situations. Indeed these danger signals might cause other experimenter controlled CSs to be less effective.

If uncontrolled odor cues serve as effective CSs (as Minor and LoLordo suggest), then the magnitude of an observed escape deficit may vary greatly. If the odors in both the shock and test apparatus are very similar then escape deficits are more likely to occur (assuming that the CR involves a freezing of motor responses). However if the odors are very different between shock and test situations then it is likely that less influence will be exerted by learning factors and smaller escape deficits or no impairment at all will result.

Minor and LoLordo(1984) suggest that other types of deficits following inescapable shock (in addition to escape learning) may also be affected by olfactory contextual cues. Of interest to the present study is the SIA that has been commonly reported to follow treatments of inescapable stress to animals (for reviews see Henry, 1982; and Druggan, Moye & Maier, 1982). Before exploring the relationship between SIA,

learned helplessness, and context further, it is first necessary to review some basic facts about how SIA is induced, defined and measured.

SIA has been demonstrated in a wide variety of paradigms using many different forms of stress. The most frequently employed form of stress in this literature is electric shock delivered to rats through the tail or feet. Other stressors have been used including cold water swims, chronic restraint, social isolation, centrifugal rotation, and interperitoneal hypertonic saline injections(for a review see Watkins & Mayer, 1982).

It should be pointed out that the temporary increase in pain tolerance that results from exposure to such environmental stimuli has been labelled "stress induced analgesia" arbitrarily. This is because stimuli such as shock and cold exposure are commonly considered stressful. However the classical definition of stress involves pituitary-adrenal activation. SIA is a misnomer since many stimuli which cause SIA do not activate the pituitary-adrenal axis (e.g. Watkins, Cobelli, Newsome & Mayer, 1982). The term "stress" however will be used herein to refer to any stimulation that induces analgesia.

The environmental stressor to be scrutinized most closely in this study is electric shock, either in the form of grid floor shock or tail shock. Shocking animals is a procedure common to many areas of psychological investigation and the parametric considerations have been a

thorny problem for some time (for a review see Campbell and Church, 1969). It is essential to detail the considerations involved in the choice of shock parameters for two reasons. First, different shock parameters have very different effects on behavior. Second, it is ethically imperative to choose shock parameters that are the minimum necessary to competently address a particular problem. It is also useful in this regard to obtain as much data as possible from each session of shock to minimize the number of animals exposed to discomfort. Investigators of SIA have also found that shock parameters radically effect outcomes. Parameters such as shock type (ac or dc), intensity, duration, frequency, method and loci of delivery, and other variables have proved very important in determining the magnitude, duration, and type of SIA induced.

For example, Lewis, Sherman and Liebeskind(1981) found that exposure to prolonged intermittent grid foot shock produced an opiate based analgesia while briefer continuous footshock induces a non-opiod analgesia. Watkins, Cobelli, Faris, Aato and Mayer (1982) found that the body region shocked is a critical factor. Footshock delivered to the forepaws causes an opiod based analgesia while footshock delivered to the hindpaws induces a non-opiod analgesia. Watkins, Cobelli, Newsome and Mayer(1982) found that tailshock induced both an opiod and non-opiod analgesia depending upon the number of shocks delivered. The parameters which have been employed in the present study

were chosen to duplicate those commonly used to induce both opiod analgesia and learned helplessness.

This study specifically addresses the issue of how associative factors may enhance the time course and magnitude of SIA. The literature describing the magnitude and time course of SIA is reviewed to provide a standard of comparison for the results of the present study. But first it is necessary to describe the methods of assessment that are used to obtain these results.

Behavioral assessment of analgesia is usually done with the tail flick procedure (D'Amour & Smith, 1941). There is, however, wide variation in the procedures and apparatus employed. These differences will be described briefly since they are related to the variations in SIA latencies reported by different investigators and therefore relevant to the interpretation of the results of the present study. For example some investigators such as Grau, Hyson, Maier, Madden, and Barchas(1981) set the intensity of the radiant heat source quite high. This intensity causes control group rats to respond quite quickly (4-6sec). Others such as Jackson, Maier and Coon(1979) adjust the heat source to allow longer control group response times (6-10 sec).

It is therefore easier to express the magnitude of SIA in terms of a ratio of the latencies of shocked rats to control rat latencies. For SIA testing up to 3 hours after inescapable shock (using learned helplessness parameters) tail flick latencies are typically inflated 70%-100% over

baseline levels (Maier, Druggan & Grau, 1982). SIA has not been demonstrated beyond 24 hours after shock unless several more shocks are administered prior to testing. These are referred to as priming shocks. For SIA testing at 24 hours after shock with the use of priming shocks (Maier, McDaniel, Jackson & Grau, 1979) tail flick latencies are inflated 50%-80% over baseline levels. These figures indicate that a test procedure that induces average baseline latencies of 8-10 seconds should result in SIA latencies of 15-20 seconds for rats tested within 3 hours of stress (Maier, Druggan & Grau, 1982) and 13 to 18 seconds for rats receiving five priming shocks 24 hours after shock (Maier et al., 1979).

It is now possible to return to the relationship between SIA and learned helplessness. Of particular interest to the present paper is the portion of this literature that examines analgesia resulting from the same inescapeable shock parameters that are used to induce learned helplessness in the rat (e.g. Minor and LoLordo, 1984).

Maier, Sherman, Lewis, Terman and Liebeskind(1983) noted that the deficits commonly seen in escape learning following inescapable foot and tail shock were paralleled by the development of SIA. Moye, Hinson, Grau and Maier (1983) confirmed this finding and further noted that SIA does not result following treatments of escapable shock. They concluded that the learning of uncontrollability seems to be necessary in the development of SIA. However it is necessary to recall at this point that Minor and LoLordo(1984) were

also able to avoid deficits following inescapable shock by manipulating contextual variables (odor). Essentially, then, Minor and LoLordo were able to interrupt or compensate for learned helplessness by changing contextual factors along the odor dimension. Thus an important question arises.

Are SIA studies vulnerable to contextual effects in the same manner as escape-avoidance learning? This question is important because SIA studies have not, to date, applied rigorous contextual controls (particularly olfactory controls). Thus the possibility exists that SIA studies, like learned helplessness studies, have also been confounded along the contextual odor dimension. That is, these studies have failed to control the contextual associative factors which may affect SIA. Thus a misleading picture of the time course and magnitude of SIA may have been obtained.

The basis of the above inference is as follows: first, inescapable shock only causes escape deficits when the contextual odor between shock and later testing environments is the same or very similar; second, inescapable shock as it is employed in learned helplessness procedures causes analgesia. Based on these assumptions SIA should be affected by contextual manipulations in the same manner that learned helplessness deficits are. That is, SIA should occur maximally when the analgesia assessment procedure is coded with the same contextual cues (especially odor) as the shock environment.

II. Experiment 1 Rationale

The above suggestion can be tested by factorially manipulating odor between shock and later analgesia measurement contexts, that is, by shocking rats in one of two distinct contexts and testing them in the same or different context. The null hypothesis is that the magnitude of SIA will be similar regardless of the odor context within which analgesia assessment is conducted. The research hypothesis is that SIA will interact with odor context such that increased analgesia will occur only when the odor context is the same or very similar between shock and later analgesia test environments.

This hypothesis was tested using a 2x2x4x2 mixed design with two between groups factors and two within groups measures. The first between groups factor was the odor present during shock with two levels: peppermint(P) or lemon(L). The second between groups factor was the odor present at analgesia assessment (P or L). The first within subjects variable was trials of analgesia test with four levels. The second within subjects factor was test sessions with two levels (2 hours and 24 hours after shock). Thus four groups of subjects were tested. Two of these groups were shocked with odor P present and the other two with odor L present. Subsequently these groups were tested for analgesia in odor contexts that were the same or different to their initial shock odor experiences, producing four odor combinations at analgesia assessment: PP, PL, LP & LL. A

control group was also included for baseline purposes. Rats of this goup received no shock and no odor exposure, but equivalent amounts of handling, restraint and analgesia testing.

A repeated measures design was selected because pilot studies revealed this to be a more stable indice of SIA. The sessions variable was also included to assess the long term effects of these manipulations. Previous studies (Maier, 1979; Maier & Coon, 1979) have revealed that long term SIA (from 3 to 24 hours) can only be obtained if the rats receive several priming shocks prior to analgesia assessment. Because contextual factors have been predicted to amplify SIA it was decided to assess the subjects again at 24 hours after shock to determine if the SIA obtained in the present study lasts longer than that usually seen in other studies in which contextual variables are not controlled. It was predicted, a priori, that the same pattern of results would occur at 24 hours after shock as would arise as at 2 hours. The only difference predicted to occur between these two sessions was that the long term effect was likely to be smaller in magnitude.

The dependent measure in this study was tail flick latency, defined as the time between onset of a high intensity light focussed on a rat's tail and a tail flick response. This response is accepted as an accurate indice of analgesia (be it induced by stress, surgical or pharmacological means) and is the most widely used procedure

at the present time for behavioral assessment. It can also be employed in procedures using tail shock provided the light is focussed on a different portion of the tail (e.g. Maier et al., 1979; Watkins, Druggan, Hyson, Moye, Ryan, Mayer & Maier, 1984).

Based on the above hypothesis the groups tested under similar odor conditions (PP and LL) will be more analgesic (longer tail flick latencies) than the groups tested under different odor conditions (PL and LP). According to this prediction no main effects for odor at shock, or odor at test would be observed. Only the interaction between these main effects was predicted to be significant.

Methods

Subjects

Forty male Sprague-Dawley rats between 55 and 65 days old (250-350grams) at the start of the experiment were obtained from the University of Alberta breeding stock. They were maintained with free access to food and water. All rats were individually housed in plastic shoe box type cages (20x20x40cm) for 10 to 14 days prior to the start of the experiment.

Apparatus

Restraint

Black plastic polyvinlychloride (PVC) tubing (8cm in dia) was cut into 15cm lengths and fitted with friction fitting end caps. The front caps had fifteen ventilation holes (0.4cm dia) and the rear caps had t-shaped slots (4x4cm) cut into them to allow the tail to protrude and move freely. The tubing was drilled with six (0.2cm dia) holes along the base to provide adequate ventilation and drainage.

Shock

Shock was delivered through tail clips friction fitted and taped to the mid-portion of the rats tail. These clips consisted of standard plastic backed fuse terminals. Prior to attaching the shock clips a plexiglas washer with a 1cm diameter hole was placed at the butt of each animal's tail and taped into place to prevent withdrawal of the tail into the tube. The position of the shock clips was marked on the tail with a felt pen for later reference. Shock leads were clipped to the fuse clips and connected to a Lafayette constant current shock source (type 6226). The shock source was set to deliver a constant current 1.0 mA AC shock by passing high voltage through a 51K ohms fixed resistor in series with the shock source and the rat. This technique insured that any changes in the animals' resistance over time would have an insignificant effect on the current. Current level was checked before and

after each shock session. The shock source was controlled by a RCA Cosmac VIP microproccesor which was programmed to manipulate shock duration, intershock interval timing, and number of shocks, and display these parameters on a video monitor. The shock was delivered inside Coulbourn Instruments sound attenuating chambers equipped with exhaust fans that also served to generate background masking noise (63db). The restraint tubes were fixed to sliding plywood bases inside the chambers. Attached to these bases were wood wedges (8x4cm) to which the rats tails' were fastened during shock. This ensured a slight elevation of the tail which prevented seepage of urine and perspiration across the electrodes. Pilot studies indicated that this precaution was essential to ensure precise shock delivery.

Tail Flick

Analgesia was assessed using a tail flick apparatus. This consisted of a 35x35cm sliding plywood tray with 2 shallow "v" slots (0.5x0.5x10cm) to center the rat tails. The restraining tubes were centered on these slots between protruding two inch finishing nails. The slots in the sliding tray could be alternately centered beneath a converging lens placed 7cm above the tray surface. This lens focussed the light from a 300 watt slide projector lamp onto either of the slots depending upon the tray position. The distance between the lens and the lamp was adjustable to modulate the

radiant heat intensity at the tray surface. Switching on the projector lamp activated a timer automatically by triggering a photocell placed between the two slots. The timer continued to run until a rat's tail was moved 3-5mm laterally or vertically, which would expose a second photocell in the base of the tail slot, which in turn would automatically stop the timer. The lamp was shut off manually. A manually operated switch was used to switch the photocell relay from the left to the right slot depending on which slot was in use. Care was taken to ensure that the radiant heat was focussed on a different portion of the tail than that where the shock electrodes were placed (as indicated by the felt pen marks).

Contextual Odors

Tailflick and shock environments were distinguished by coding the tubes with different odors. Peppermint and lemon extract (Empress Foods Ltd., domestic food preparation type) were selected for this purpose. Approximately 4ml of the odors were applied by eyedropper to a 6x13cm piece of paper towelling taped snugly over the front end of the restraint tube. To ensure that these potent odors were controlled adequately, special precautions were employed. Two separate labs removed from the housing area were used exclusively for each odor to ensure that lingering odors would not confound the context variable. Furthermore,

all apparatus and experimental work surfaces were cleaned periodically to remove lingering odors. The restraint tubes were thoroughly cleaned after each rat by first soaking the tubes in a warm water bath of Organisol, then washing in a bath of Alconox and finally rinsing in hot water before air drying.

Procedure

Handling

Prior to the start of the experiment all rats received handling to adapt them to the experimenter and apparatus employed. Pilot research indicated that this handling was necessary to avoid a short term 'behavioral' analgesia that caused increased variability in the data and interfered with interpretation of the effect of interest (SIA). This handling took place over five sessions. In the first session the rats were merely removed from their homecages and handled for a minute or two. In the second session the rats were weighed and given slightly more handling. In the third session the rats were placed in the tubes for several minutes. The fourth session involved placing the animals in the tubes and taping the tail disks in place to prevent withdrawal of the tail. The fifth session repeated this procedure and involved leaving the animals restrained in the tubes for approximately 45 minutes. At the end of this phase of the experiment all rats could be handled and loaded

into the tubes with no difficulty.

Tail Flick

Prior to the start of the experiment the tail flick apparatus was calibrated using several naive animals. The distance between the lamp and the condensing lens was adjusted such that tail flicks occurred after approximately 7-10 seconds of radiant heat stimulation. The tail flick procedure consisted of first placing two rats into the restraint tubes and placing the tubes onto the sliding tray such that the rat tails lay in the slots. Two minutes later the first trial began. A trial consisted of manually turning on the lamp and waiting for the rat to move his tail. At that point the lamp would be manually shut off, the latency recorded, the timer reset, and the photocell relay would be switched over to the other slot. The tray was then slid over until the second tube was correctly centered. This procedure was repeated with a two minute intertrial interval for a total of four trials for each rat. If an animal moved its tail out of the slot 30 seconds before or less than one second after the lamp came on the trial was aborted and redone two minutes later. This type of event is referred to as a false start and was recorded. After each trial the rat's tail was placed back into the slot by the experimenter, and replaced if the tail was moved out of the slot up to 30 seconds before the next trial. Otherwise the rats and their tails were not

handled at all during the tail flick procedure.

Baseline

A control group of eight rats was run first. These animals received five sessions consisting of four tail flick trials separated by approximately 24 hour intervals. They were not tested in the presence of peppermint or lemon and were merely restrained for an amount of time equivalent to the rats in the other experimental groups.

Experiment 1

Thirty-two rats were randomly assigned to four groups. Prior to Day 1 of the experiment all groups received a single session of four tail flick trials. Pilot studies revealed that the first session of tail flick trials tended to be quite variable and latencies quite slow, however, subsequent sessions of trials were much less variable and latencies were faster. Thus all groups received this first session of trials to filter out this "noise". These data were recorded but not included in the main analysis. Day 1 of the experiment involved shocking the rats. Two groups received shocks in the presence of the peppermint odor and the other two groups were shocked in the presence of the lemon odor. All groups were otherwise treated in precisely the same manner. Shock intensity was 1.0mA and shock duration was five seconds. A total of 80 such shocks were delivered

on a random time interval (range 30 to 90 seconds). A three minute adaptation period preceded the delivery of the first shock. Immediately after the last shock the rats were removed from the restraint tubes and returned to their homecages which in turn were returned to the housing room. Two hours later the rats were returned to the experimental rooms for tail flick testing. Half of the rats were tested with the same odor present during shock (groups PP and LL). The other half of the rats were tested with the odor not present during shock (groups PL and LP). These four groups received four trials on the tail flick apparatus with a two minute intertrial interval (ITI) and a two minute adaptation period preceding the first trial. Approximately 24 hours later all groups were given a second session of tail flick trials with the same parameters.

Results

The control group data were analysed using a repeated measures analysis of variance with two factors: trials (4) and sessions (4). (See Appendix 1 for the source table.) The sessions effect approached significance $F(3,21)=3.463$, $p<.053$. A Newman-Keuls means comparison test specified the location of this effect to be between the first session and the other three sessions which did not differ from each other, $p<.05$. These means are displayed in Figure 1. Tail flick latencies for all shock groups were analysed in a

2x2x4x2 (shock odor x test odor x trials x sessions) mixed analysis of variance (see Appendix 2). The means for this analysis are displayed in Figure 1 also. The predicted interaction effect did not attain statistical significance. However four other effects of interest were obtained. A significant main effect for sessions was obtained, $F(1,28)=5.323$, $p<.03$. Newman-Keuls means comparisons tests confirmed that tail flick latencies at 24 hours were longer for all groups, $p<.05$. The test odor by trials interaction was significant, $F(3,84)=4.355$, $p<.02$, and is graphed in Figure 2. Newman-Keuls means comparisons revealed that subjects tested under the lemon odor conditions (PL,LL) had significantly longer response times on the fourth trial ($p<.05$) than the rats tested with the peppermint odor (LP, PP). A significant trials by sessions effect was also obtained, $F(3,84)=6.987$, $p<.01$. The means for this interaction are displayed in Figure 3. Means comparisons specified the source of this effect to be between response times on Trial 1 at 2 hours and 24 hours with the latter being slower. Finally, a triple interaction occurred, $F(3,84)=3.988$, $p<.05$. Mean comparisons revealed that tail flick latencies for groups tested with lemon were significantly longer on the fourth trial of the first session of trials, $p<.05$. The means for this triple interaction are graphed in Figure 4.

These data were also analysed to compare the performance of the four shock groups to the baseline group.

These combined data were analysed by a 5x4x2 mixed analysis of variance (groups x trials x sessions) and are contained in Appendix 3. (The means for this analysis are displayed in Figure 1.) This resulted in a significant groups effect, $F(4,35)=16.45$, $p<.0001$. Newman-Keuls means comparisons revealed that the no shock group was significantly quicker than all of the other groups, $p<.05$. A significant groups by trials effect was also obtained, $F(12,105)=2.042$, $p<.05$. Means comparisons revealed that animals tested with the lemon odor had latencies that increased over trials while the latencies of the other groups tended to remain steady, $p<.05$. The trials by sessions interaction was also significant, $F(3,105)=6.036$, $p<.017$. Means comparisons revealed that performance on Trial 1 was faster in Session 2; otherwise all of the other trials were not significantly different across sessions, $p<.05$. Finally, the record of false starts during tail flick testing revealed less than 3% of all trials were aborted (with an even distribution of false starts in each of the groups).

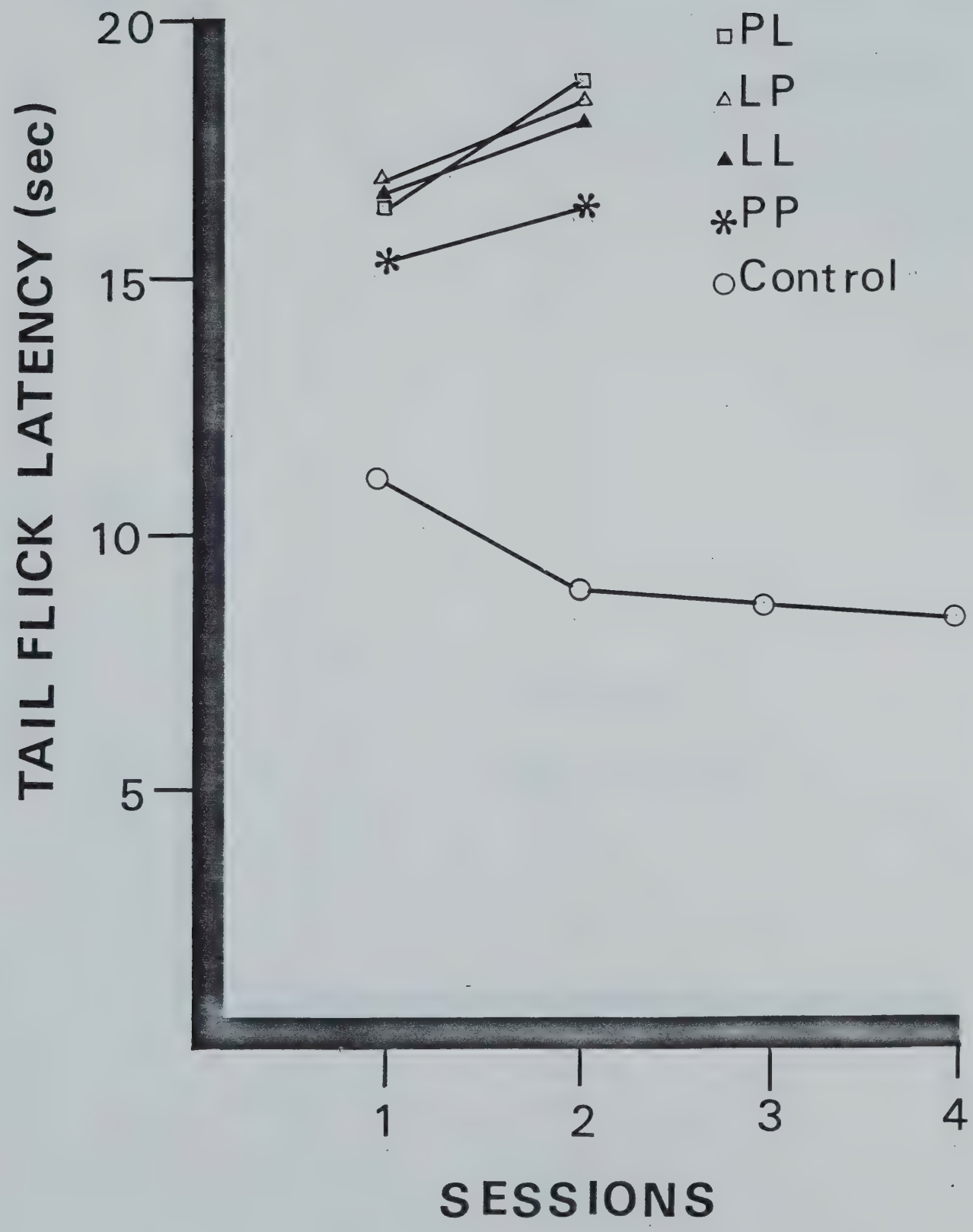

FIGURE 1. EXPERIMENT 1 SESSION x GROUPS INTERACTION

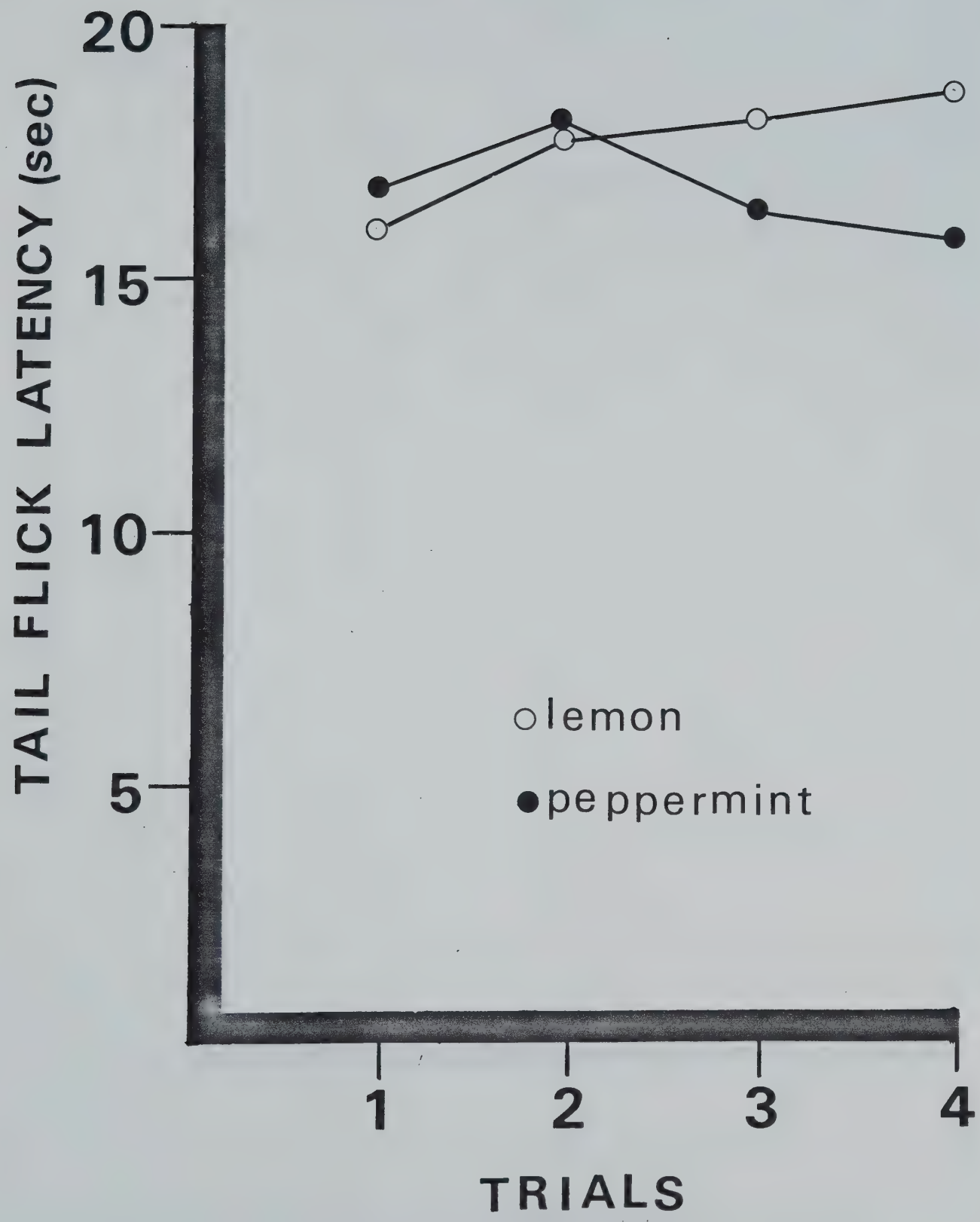

FIGURE 2: TEST ODOR x TRIALS INTERACTION

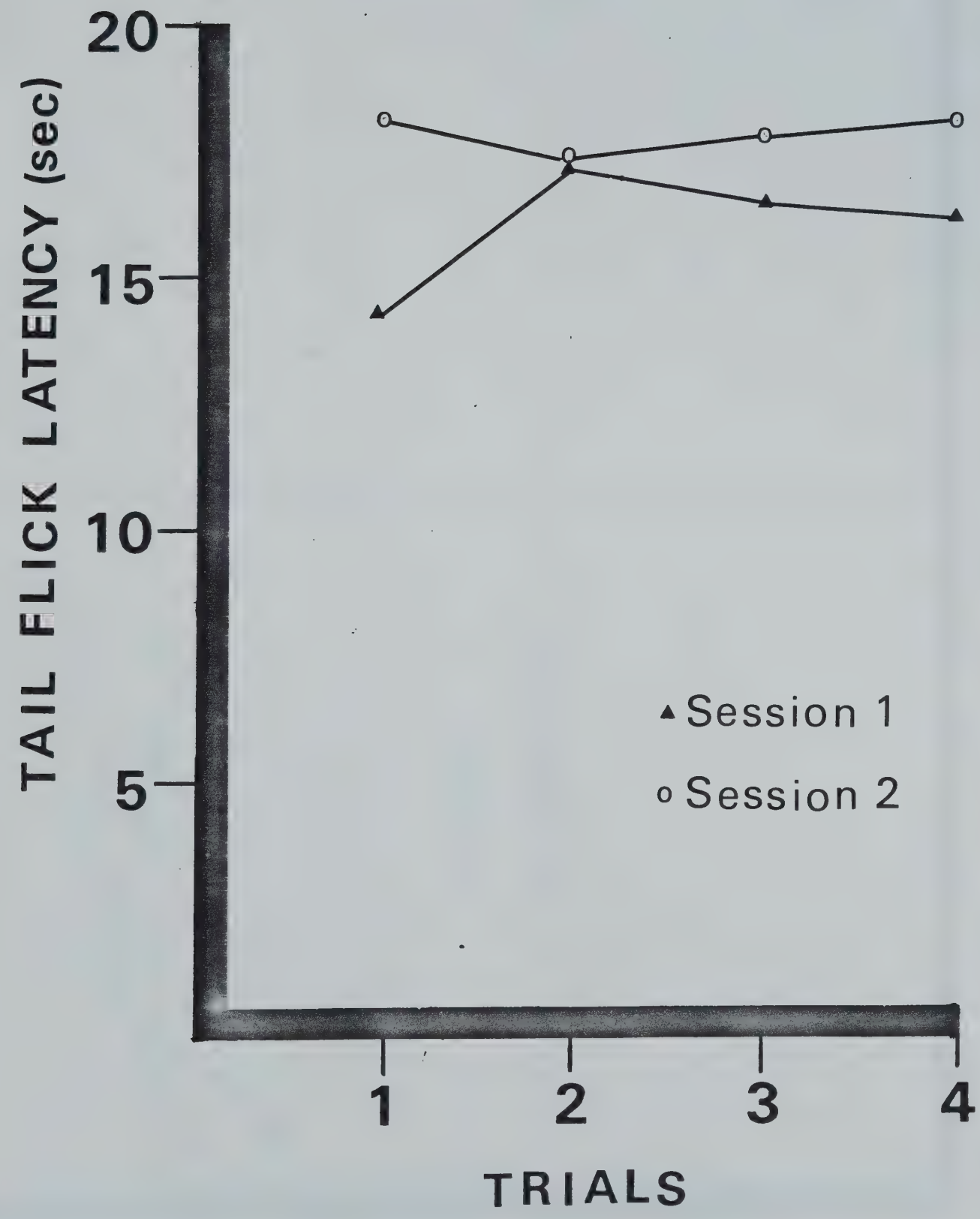

FIGURE 3; SESSION x TRIALS INTERACTION

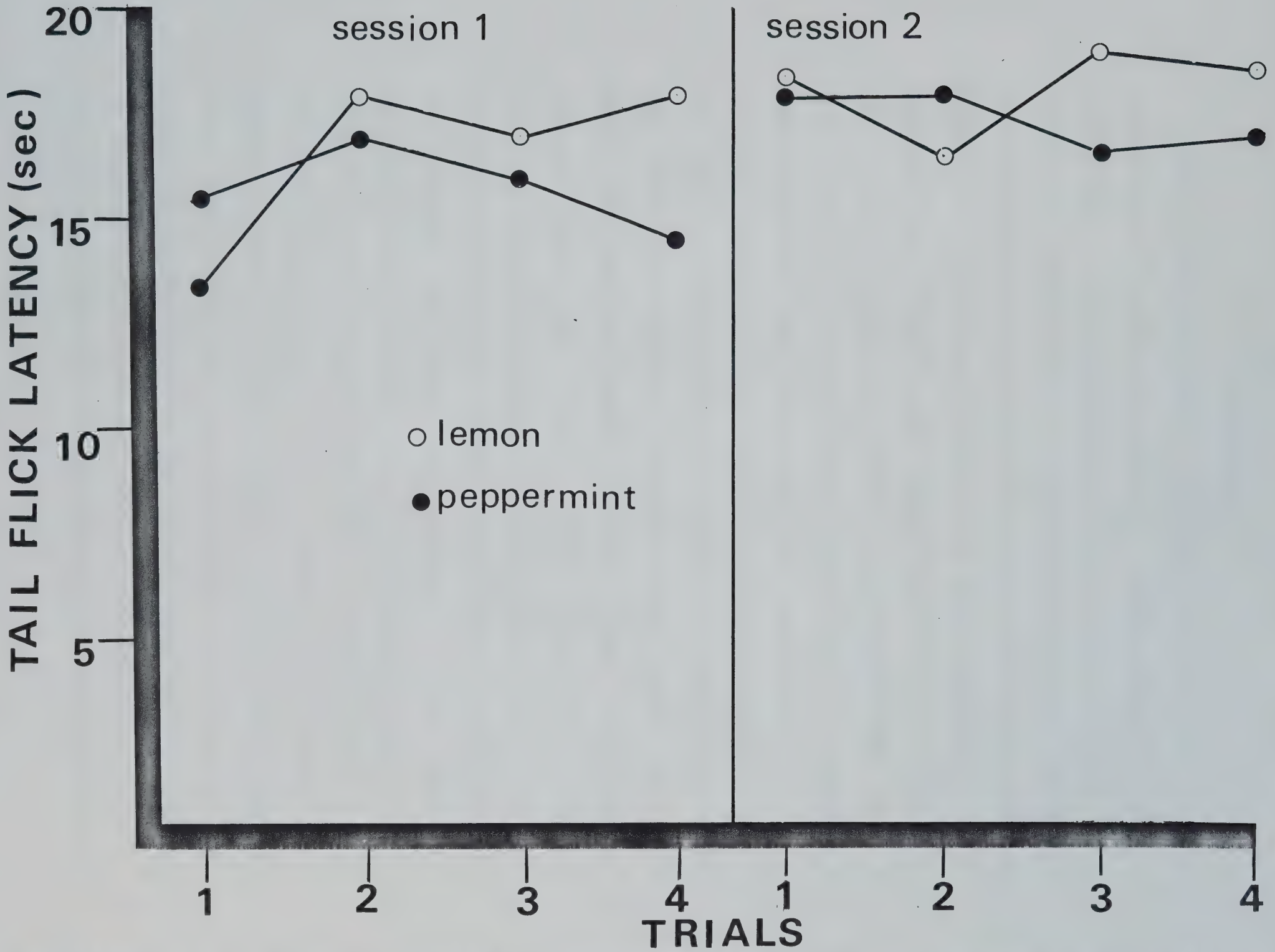

FIGURE 4; TEST ODOR x SESSION x TRIAL INTERACTION

Discussion

One of the predicted results was obtained. The comparison of the four groups that received shock (PP, PL, LL, LP)with the no shock control group revealed a very robust SIA. However none of the odor combinations was more or less analgesic than any of the other groups that received shocks in a scented environment. The major research hypothesis was therefore not supported with the present data. Thus the suggestion of Minor and LoLordo(1984) that other types of inescapable shock induced deficits may come under contextual odor control was not supported.

The significant sessions effect which revealed increased tail flick latencies at 24 hours after shock also runs counter to existing literature. Grau, Hyson, and Maier(1981) have been unable to obtain long term analgesia (between 3 hours and 24 hours) in the absence of priming shocks. This unusual pattern of results was also reflected by the two way interaction between trials and sessions. In that instance tail flick latencies on Trial 1 in Session 1 were much quicker than on Trial 1 in Session 2. The literature concerning the time course of nociceptive deficits does not contain such a finding. Maier(1979), for example, presents data which show a shock primed analgesia effect at 24 hours that disipates by 48 hours. However the trials by sessions interaction was not significant. Indeed in the Maier(1979) and other similar studies the relationship between trials and sessions tends to be in the

opposite direction of the present data,with performance in later sessions dropping off drastically on all trials.

The two way interaction between test odor and trials suggested that the lemon odor was responded to more effectively. Testing under the lemon odor yielded longer response times on the fourth trial only (although this difference approached significance also on the third trial). A similar pattern of results was reflected in the three way interaction. In this instance the source of the interaction was performance on Trial 4 in Session 1. Again, animals tested with the lemon odor were much slower than those tested with peppermint, but only in Session 1; 24 hours later peppermint and lemon test results were not significantly different. In both these instances it is pertinent to ask if the lemon and peppermint odors were equally salient? One possible explanation for these two interactions is that peppermint odors leaked from the peppermint lab into the housing area (these rooms were adjacent). Thus analgesia responses to the lemon odor may have been partly extinguished. However this explanation fails to explain why the peppermint-lemon difference is not evident in Session 2.

It is difficult to determine, in a post-hoc fashion, the cause of the peppermint-lemon response differences. Future experimentation could evaluate the relative salience of these two scents in a conditioning procedure. For the moment it is best to examine the most surprising aspect of

these results- the long term analgesia.

This experiment was designed essentially to extend the findings of Minor and LoLordo(1984). However, certain differences in procedures exist between that study and the present study. Minor and LoLordo shocked the rats in wheel turn chambers or restraint tubes and later tested in operant chambers or shuttle boxes. In the present study shock and testing occurred in the same chambers (PVC restraint tubes). Thus Minor and LoLordo employed different chambers with same or different odors in them while the present experiment used the same chambers with same or different odors in them. Clearly a difference exists here. The odor cues may be more salient, then, when common apparatus cues that a rat can discriminate are missing (e.g. apparatus shape, texture, lighting).

This possibility has some theoretical support. The Kamin blocking effect (Kamin, 1968) may be useful in understanding why odor cues were not as salient in the present study as in Minor and LoLordo(1984). Blocking refers to the reduced development of stimulus control by one of two covarying cues caused by prior discriminative learning with one of the cues. In the present instance the apparatus cues may have served as associative "sponges" and left little analgesia for the odor cues to be associated with. Thus in subsequent tail flick testing the signal value of odors is blocked out by apparatus cues common to shock and test situations. In the present experiment no pairing of shock

and restraint tube occurred unless odors were also present, however the tube cues may have 'overshadowed' the odor cues and thereby more effectively absorbed the conditioning that the UCS could support. MacKintosh(1974, p47-51) described the important aspects of CSs that determine which of two or more competing CSs will 'overshadow' other CSs. This posibility leads to a second experiment.

III. Experiment 2 Rationale

If the results of Experiment 1 were due to the blocking of odor by apparatus cues, then changing these cues should significantly alter the observed analgesia magnitude. The null hypothesis in this case was that analgesia magnitude does not fluctuate when different types of apparatus are employed. Different apparatus types refers to gross contextual differences in the restraint apparatus. The research hypothesis is that tail flick latencies will be reduced substantially when the apparatus is different from that employed during shock.

In order to assess the contribution of odors to the PVC tube context these tubes were employed with and without odors. If the tube design itself is largely prepotent the PVC tubes coded with no odors should be as effective in inducing analgesia as PVC tubes with odors. However if odors supplement the contextual dimension then PVC tubes with odors should induce more analgesia than scentless tubes. Furthermore, tubes scented with the same odor used during shock should induce more analgesia than tubes scented with the odor not employed during shock.

The above hypothesis was testing using in a 4x4x3 mixed analysis of variance with one between groups variable and two within subjects variables. The between groups factor was type of restraint tube with four levels. The first within subjects variable was trials of tail flick testing with four levels. The second within subjects variable was sessions (at

72, 96 and 120 hours after shock). Tube types were either the same restraint tubes as in Experiment 1 or a different type constructed from wire mesh to be described below. The PVC tubes were used in 3 ways: without odors or with the same or different odors in the presence of which the rats were previously shocked. The wire mesh tubes were not scented. Thus the four tube types were: PVC tube with same odor as shock, PVC tube with different odor than shock, PVC tube with no odor, and mesh tube with no odor.

The dependent measure is the same as in Experiment 1. Based on the above hypothesis, tail flick latencies for the mesh group should be much lower than the other three groups combined. The tailflick latencies for the three PVC groups are predicted to be different from each other The no odor group should be quickest, the same odor group the slowest, and the different odor group will fall between these two groups.

Methods

Subjects

The rats used in Experiment 1, except for the control group rats, were continued in Experiment 2.

Apparatus

The apparatus was the same except for the wire mesh tubes. These consisted of a 24x24cm piece of insect

screening sewn into a tube shape and fitted with a zipper along the length to permit easy loading of rats. One end of the tube was sewn shut and the other left open. Paper towelling was stuffed into the closed end to adjust the tube length appropriately.

Procedure

The rats were assigned to each of the four apparatus groups. Complete randomization was not employed because it was necessary to assign half the rats according to their odor histories in Experiment 1. Eight rats were asigned to be tested in the presence of the same odor that was present during shock in Experiment 1 (4PP and 4LL). The remaining eight rats were assigned to be tested in the presence of the odor that was not present during their shock session (4PL and 4LP). The other half of the rats were assigned to the no odor tube and mesh groups randomly. Otherwise the testing procedure was the same as employed in Experiment 1. The only other difference involved the mesh tube group. Since the mesh tubes did not have end caps rats were prevented from backing out of the tube by the experimenters fingers which were placed over the opening astride the tail. The same plexiglas washers were placed on the tails; however, they were not taped into place.

Results

Data for Experiment 2 consisted of three additional sessions of trials at 72, 96 and 120 hours after shock. These data were analysed in a 4x4x3 mixed analysis of variance (groups x trials x sessions). This source table is contained in Appendix 4. A significant main effect for groups was obtained, $F(3,28)=3.748$, $p<.05$. Three planned comparisons based on the above predictions were carried out to isolate the source of this significant groups effect (see Figure 5). The first comparison found the combined scented tube groups (same and different odor as shock) to be significantly more analgesic than the combined mesh and no odor tube groups, $p<.0142$. The second comparison failed to discriminate the same and different odor tube groups from each other, $p<.6051$. The third comparison just failed to find the no odor tube group to be significantly more analgesic than the mesh group, $p<.0516$. The source table for these comparisons is contained in Appendix 5. A significant effect was also obtained for trials, $F(3,84)=4.649$, $p<.012$. Means comparisons specified the source of this variance to be between Trials 1 and 3, with Trial 3 being quicker (see Figure 6). Finally there was a significant main effect for sessions, $F(2,56)=4.934$, $p<.012$. Newman-Keuls means comparisons revealed the source of this variance to lay between Session 1 and the other two sessions combined, $p<.05$. At 120 hours after shock response times were significantly lower than at 72 hours after shock. These

means are displayed in Figure 7. The groups x session interaction was not significant, $F(6,56)=.9576, p<.4622$. However these means are displayed in Figure 8 along with the means from Experiment 1. This was done to present a complete picture of SIA in Experiments 1 & 2 over five sessions (with 24 hours separating each session except sessions 2 and 3 which were separated by 48 hours).

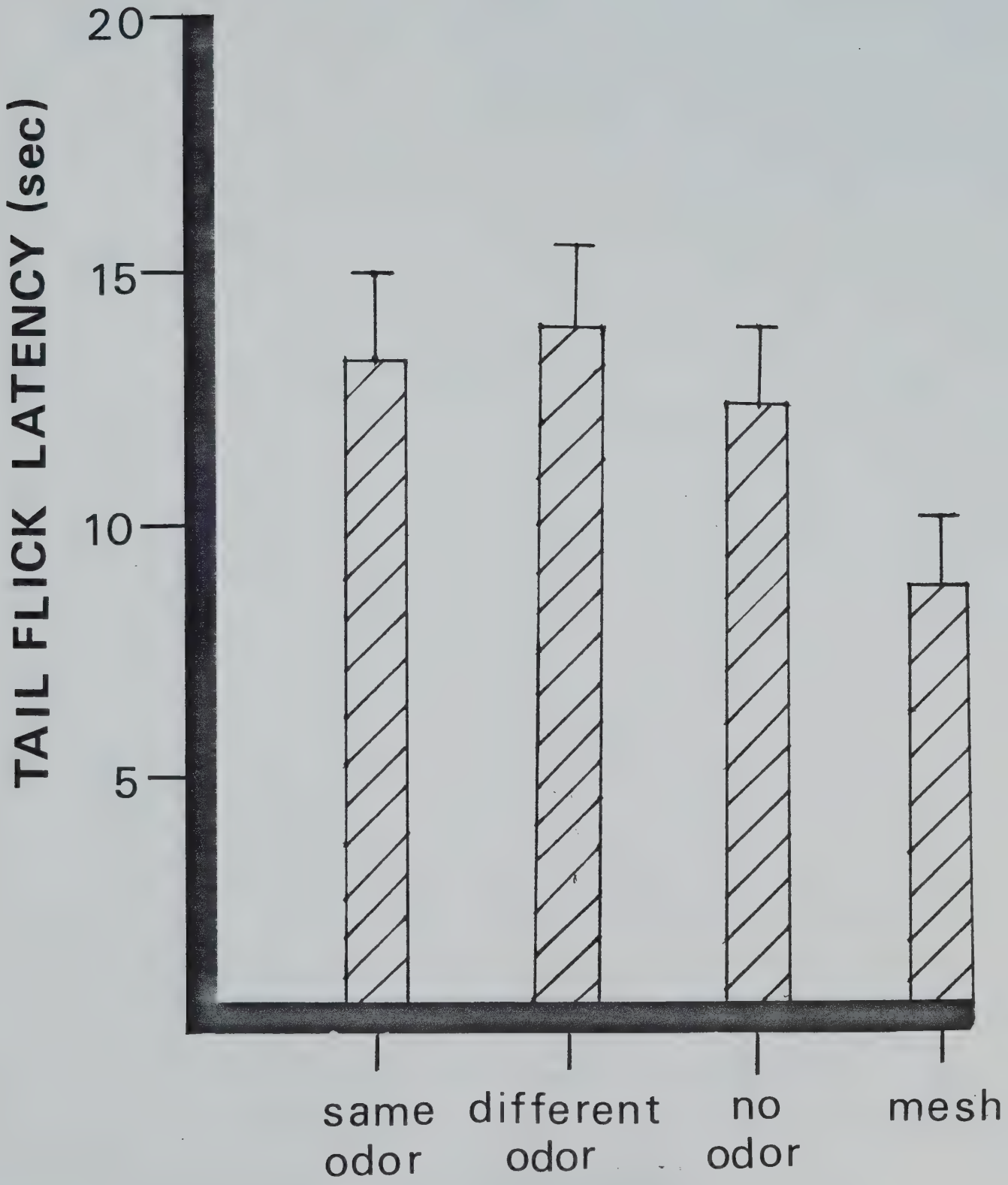

FIGURE 5; GROUP EFFECT

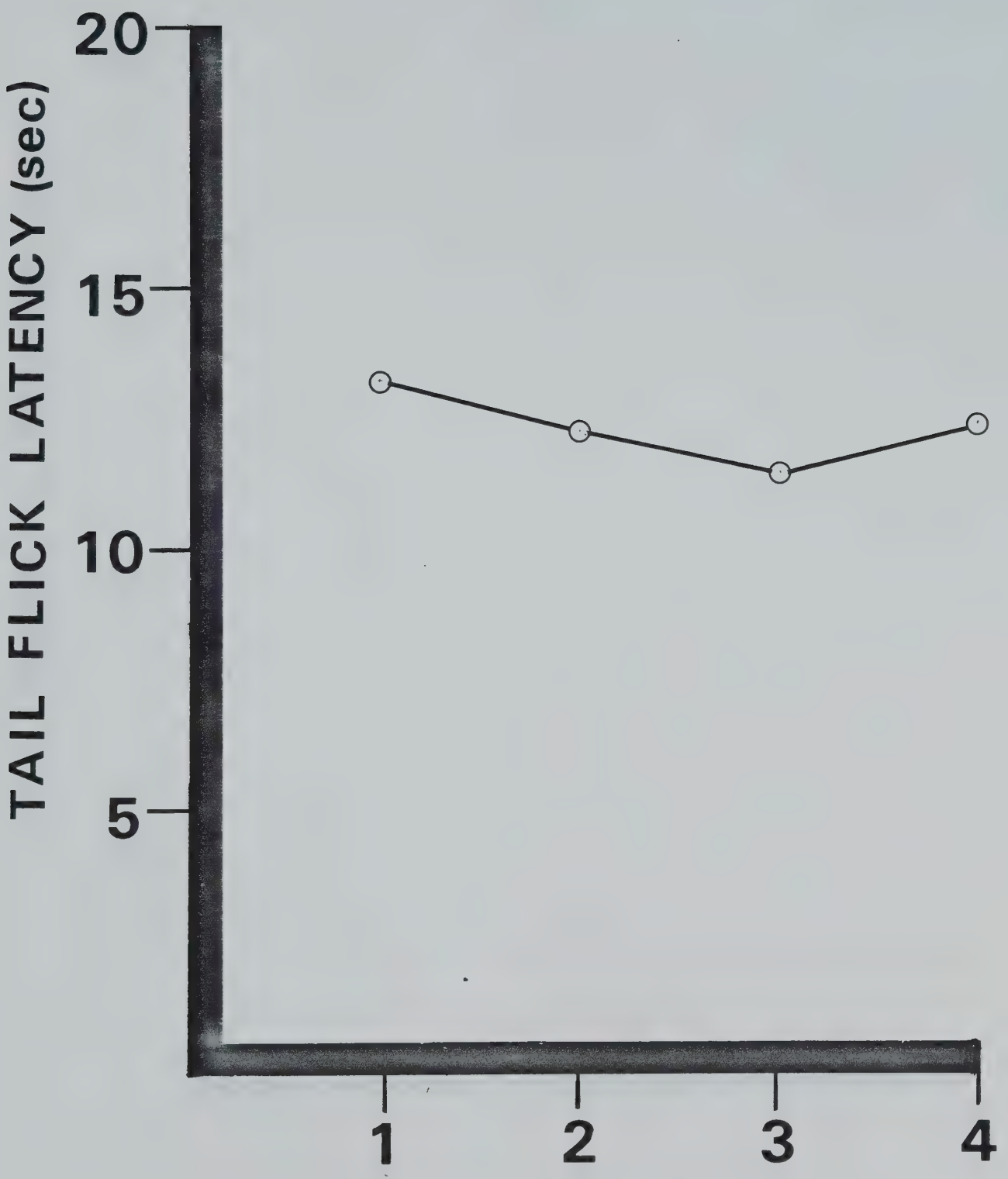

FIGURE 6; TRIALS EFFECT

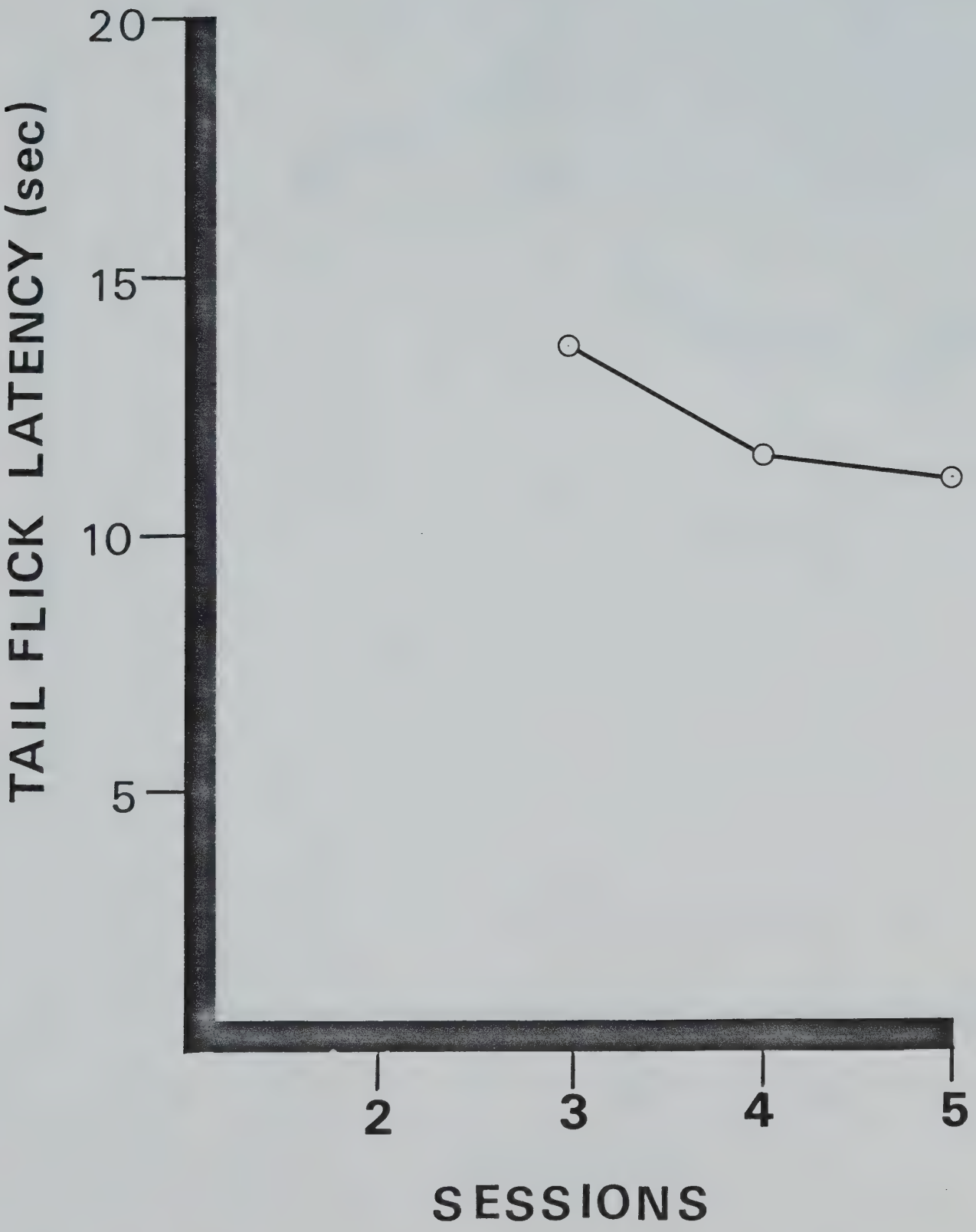

FIGURE 7: SESSION EFFECT

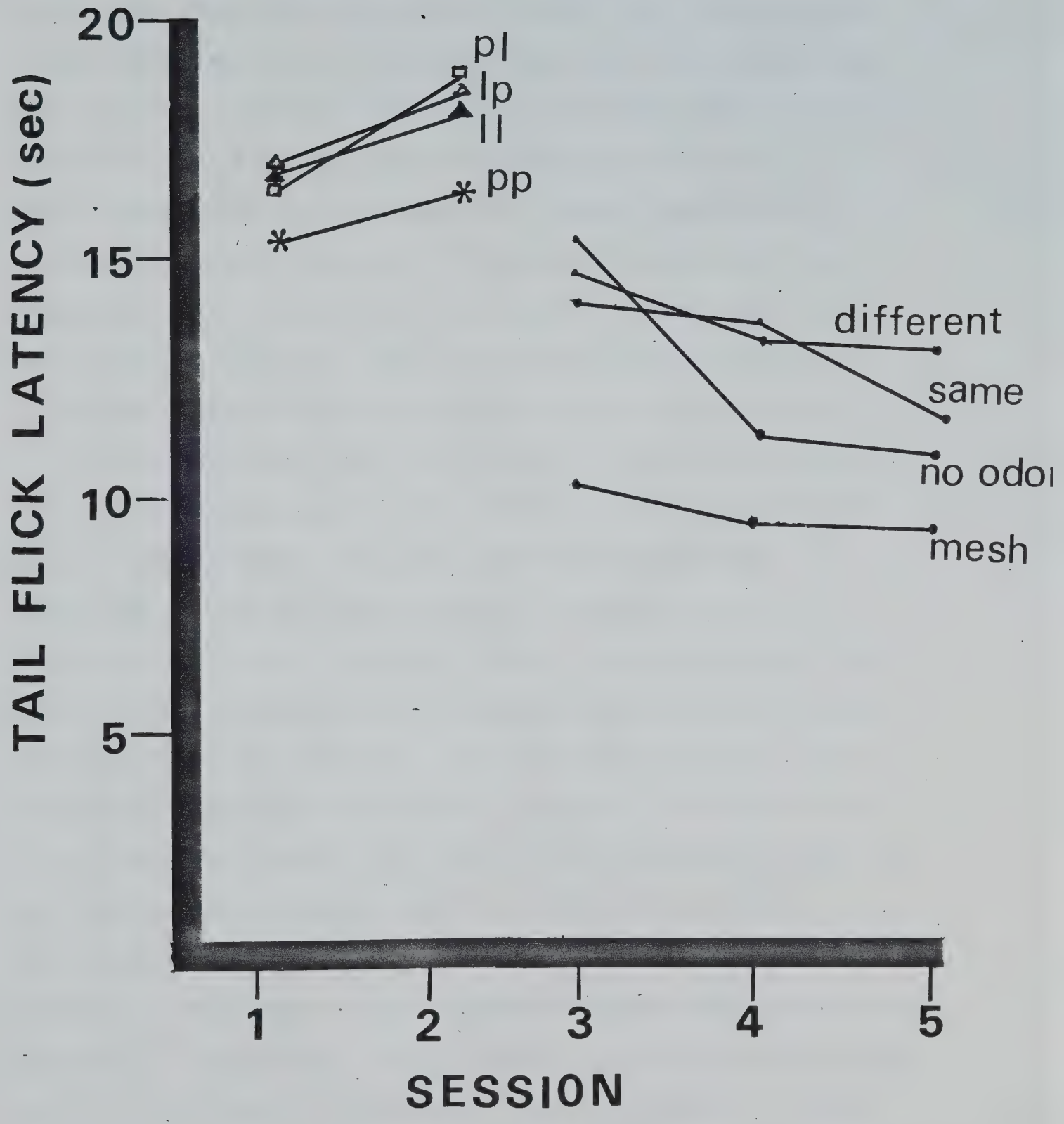

FIGURE 8: COMBINED RESULTS

Discussion

The rats that received their last three sessions in the mesh tubes responded much more quickly than the two odor groups combined. Thus, the major hypothesis was supported. This finding supports the Minor and LoLordo(1984) finding that contextual disimilarity between shock and test environments can disrupt deficits normally seen after inescapable shock. However in this study apparatus cues appeared to be more salient than specific odor cues. That is, changing apparatus cues lowered tail flick latencies significantly more than changing or removing odor cues.

The prediction that differences in odor context among the three PVC tube groups are related to the magnitude of tail flick analgesia was only partially supported. The magnitude of the obtained analgesia did bear some relationship to odor context (one of the three predictions was strongly supported and a second just slightly exceeded the 5% criterion). That is, the same and different odor groups combined had the longest latencies and the no odor tube group was almost significantly more analgesic than the mesh group. There may be some indication here that a positive relationship exists between the quantity of cues present in the test situation and the magnitude of observed analgesia. Considering the extremely long time between shock and test employed in Experiment 2 and the narrow range of latencies, it is difficult to demonstrate a clear separation between the four groups. However, there does appear to be a

clear separation between the combined mesh and no odor PVC tube groups and the combined odor PVC tube groups, and a less clear separation between the mesh and no odor PVC tube groups.

Caution must be excercised in generalizing the results of Experiment 2. This caution is largely due to the post-hoc improvisations that were made after Experiment 1 to permit further data collection. This improvisation places certain constraints on Experiment 2. The first is that because all of the rats were previously run in Experiment 1 they experienced six sessions of tail flick trials over 7 days in total. This is more than commonly reported and therefore could be considered more stressful and likely to inflate SIA (due to repeated stimulation of the tail and repeated restraint sessions in the tubes). Second, the wire mesh tubes were introduced to some of the rats in only the last three sessions. Hence this group had less exposure to this type of tube than the other groups had to the PVC tubes. Third, the mesh tubes were not used during shock preventing the demonstration of an interaction between shock and testing apparatus. Fourth, the assignment of subjects to groups in Experiment 2 was not fully randomized and therefore violates some statistical assumptions. Fifth, the baseline control group data was not collected at 96 and 120 hours after shock (although this group appeared to have reached a stable level after four sessions of testing). Nonetheless, the data obtained do have some merit,

particularly in interpreting the unusual results of Experiment 1.

The second of these points is intriguing in light of pilot work, which revealed that novel apparatus usually cause a temporary increase in response latencies referred to as "behavioral analgesia". Bardo, Wellman and Hughes(1981), and also Bardo and Hughes(1979) reported a similar phenomenon in hot plate analgesia testing. Based on this literature, a change of tube context should have slowed responding slightly for this group. However the absence of apparatus cues normally associated with shock was enough to compensate for the slight behavioral analgesia that novelty tends to induce.

IV. General Discussion

Taken together the results of these two experiments demonstrate that the time course and magnitude of SIA can be altered significantly by manipulating contextual variables. It is not clear however exactly what the nature of these variables must be. Experiment 2 demonstrated that a return to baseline levels could be accelerated by introducing a new tail flick test environment. However it is possible that introducing this new test apparatus late in the procedure could disrupt analgesic responses in a manner confounded with context. Perhaps, for example, it is easier for a rat to make tail flick responses in a wire mesh sock than a PVC tube. This possibility could be discounted by introducing both types of test apparatus at the beginning of a study such as the present.

An improved experimental design would entail using two very different types of restraint tubes analogous to the manner that odor was manipulated in the present study. Thus, at the start of the study, half of the rats would be shocked in the wire mesh tube and the remainder in the PVC tubes. Subsequently the rats would be tested in the same or different tube. In this way the effect of interest, the interaction, could be separated from the possible artifacts contributed by a particular tube design. It would then be feasible to go on to evaluate a possible four way interaction between apparatus type at shock, apparatus type at test, odor at shock, and odor at test. In this way, the

blocking and overshadowing effects discussed above could be more adequately dealt with.

The importance of these changes bear emhpasis since no studies to date (including Minor and LoLordo, 1984) have controlled for contextual cues in a manner that involves both apparatus and odor cues. In fact a review of the tail flick analgesia literature reveals that there is usually a very gross difference in contexts between the stress and test environments. For example Maier, Druggan & Grau(1983) conduct tail flick analgesia tests by restraining the rats in an experimenter's hand.

This type of procedure is particularly suspect because much room exists for assessment error. Pilot work revealed this technique to be a very poor indice of SIA. Rats tend to respond much more quickly when they are tested this way. These observations support the findings of the present study because an experimenter's hand is obviously a very different context than a restraint tube or shock chamber. Thus, these types of procedures are far less likely to produce a long term SIA without the added help of priming shocks. Having considered the present shortcomings and solutions it is now necessary to consider the relevance of these findings to related literature.

This will be done by reconsidering the most remarkable aspect of the present findings, the long term analgesia. The important question here is how far can one go with this type of analysis? What are the limits to the magnitude and time

course of SIA? This question is important for many reasons, the two most important being the practical usefulness of SIA for clinical problems in particular, and the implications for our understanding of pain perception and sensory habituation in general. These questions will be approached by considering SIA from an evolutionary perspective. Recall that earlier in this paper reference was made to a possible role for contextual stimuli as danger signals. From an evolutionary point of view the present results could be interpreted as reflecting such anticipatory responding to threatening and subjectively unpleasant stimulation. Freud(1936, p.149) was one of the first to suggest this when he defined anxiety.

> "Now it is an important advance in self protection when this traumatic situation of helplessness (discomfort) is not merely awaited but forseen, anticipated. Let us call the situation in which resides the cause of this anticipation the danger situation; it is in this latter that the signal of anxiety is given. What this means is this, I anticipate that a situation of helplessness(discomfort) will come about, or the present situation reminds me of one of the traumatic experiences which I have previously undergone. Hence I will anticipate the trauma; I will act as if it were already present as long as there still is time to avert it. Anxiety, therefore, is the expectation of the trauma on the one hand, and on the other, an attenuated repetition of it"

Whether or not Freud would consider the present study a rat analogue of anxiety is a moot point. The significance of Freud's remarks lay in the evolutionary perspective they reveal. It could be argued that an organism that could selectively learn to tolerate otherwise unavoidable pain would have a survival advantage in that coping resources

could be conserved for such activities as escaping the noxious stimulation at the first opportunity.

The key point here is that anticipation of a situation of uncontrollable discomfort (or responding before the fact) cannot involve a judgement of the contingencies involved in the actual situation (during the fact). Anticipation requires judging the similarity of a situation to one where the contingencies were painfully clear. Thus similarity of situations becomes the prepotent variable. If this analysis and supporting evidence are true then a number of predictions can be made.

First, controllable shock should not prevent SIA (and possibly learned helplessness) from occurring if it is experienced in an environment that is very distinct from a subsequent environment in which uncontrollable shock is experienced. This prediction runs counter to much of the learned helplessness literature, which has examined the immunization effect of controllable shock treatments. It has found been found (Maier, Drugan & Grau, 1982) that initial experiences with controllable shock prevent learned helplessness deficits and SIA following subsequent treatments of uncontrollable shock. However none of these studies have rigourously controlled the context. Thus a study is called for in which context (both apparatus and odors) are factorially manipulated between three treatments: controllable shock, uncontrollable shock, and escape learning or analgesia test.

Second, if similarity of context between shock and tail flick environments serves to trigger responses that are analgesic in nature or otherwise interferes with tail flick responding and escape learning, then the possibility of pharmacological manipulation of the context effect exists. It is common practice to reverse SIA by injecting opiate antagonists (e.g. Mah, Suissa and Anisman, 1980). Thus, it would be predicted that contextual stimuli previously associated with shock will not induce analgesia if the rats are injected with an opiate antagonist such as naloxone. However if this analgesia is neurally rather than hormonally mediated this intervention will likely not be effective.

Finally, the effects of drugs known to enhance or inhibit analgesia (eg: morphine and naloxone) should be attenuated or amplified by manipulating context appropriately. A small dose of morphine, for example, should be amplified by exposure to contextual cues previously associated with shock.

All of these predictions and associated studies are designed to challenge the unexpected long term SIA noted in the present study. The cornerstone of Freud's theory of psychopathology was anxiety- the anticipation and repetition of a traumatic event. Freud suggested that anxiety had a very long time course indeed. SIA, however, has typically been thought of as a short term phenomenon. It is clearly too presumptious, with the present data, to construct a solid bridge between Freud's concept of anxiety and SIA.

However, other research avenues exist which may provide techniques for amplifying SIA and thereby provide a better understanding of the relevant variables. The final prediction made brings up the relationship between this study and the literature that examines the associative basis of responses to drugs that are externally injected into an organism.

Siegal(1976, 1977, 1979, 1983) has reported a series of studies demonstrating that contextual factors associated with drug injection may significantly accelerate or inhibit the onset of drug tolerance acquisition. Contextual factors in these experiments involve the experimental ritual preceeding drug injection (removal from the homecage, transport to the laboratory, restraint, injection).

Siegal has employed principles of classical conditioning in the manipulation of environmental cues associated with drug injection. In these experiments it was reported that the contextual cues associated with injection of opiates serve to elicit CRs called compensatory responses. These responses are physiological responses that counteract the central effects of injected drugs. Thus in the case of morphine, which induces respiratory suppression, one of the compensatory responses is hyperventilation. Hence contextual stimuli trigger CRs that are defensive and adaptive in nature. The present study may parallel Siegal's work in these respects.

In the present study contextual stimuli associated with noxious stimulation have been demonstrated to prolong SIA significantly. It may well be that the main difference between the present approach and that of Siegal is source of the opiates- endogenous versus exogenous (if in fact opiate activity subsume these processes). Future exploration of these potential similarities could therefore profitably examine some of the avenues taken in studying context and exogenous opiate treatments.

In particular, Siegal (1977) has demonstrated how the Pavlovian principles of partial reinforcement and latent inhibition can be used to manipulate and describe drug tolerance acquisition functions. A similar approach to SIA could further clarify the relationship between SIA and the work of Siegal. For example, would it be possible to eliminate or minimize the context effect in SIA by repeated exposure to the shock environment prior to shock (latent inhibition)? This possibility is intriguing in light of the adaptation procedures which were employed in the present study to facilitate ease of rat loading into the PVC tubes and eliminate behavioral analgesia. PVC tube exposure prior to shock might latently inhibit the tube cues and allow for odor cues to become relatively more salient. Thus the possibility exists that odor cues might influence SIA if more latent inhibition of tube cues was induced. Alternately, would shock sessions interspersed with non-shock sessions result in attenuation of the context

effect (a partial reinforcement effect)?

Clearly, many possibilities exist for the amplification and manipulation of SIA. One final body of literature bears mention in this regard. It should be recalled that the present research was stimulated by studies examining contextual control of shock motivated escape-avoidance performance (i.e. Minor and LoLordo). Other variables which radically affect avoidance learning have been isolated and are worth reviewing in light of the importance of context.

Levis(1966), and Boyd and Levis(1976), have demonstrated that avoidance behavior can be acquired far more rapidly and made much more resistant to extinction if a one way signalled escape-avoidance procedure is employed. Additionally the employment of compound CSs increases the resistance to extinction of this learning to the point of "superconditioning". This type of paradigm has many interesting implications for SIA studies.

Levis(1966) points out that an animal in a two way escape-avoidance situation is forced to spend time in a situation (context) preceding shock that is not much different from the situation following shock. This results in two impediments to learning. First the subject experiences less reinforcement for escaping a particular situation (since both sides of the shuttle box are very similar). Second, extinction of avoidance responses is accelerated by the presence of feared contextual stimuli during the ITI. These impediments may also exist in the SIA

procedures employed in studies such as the present. What would happen to the magnitude and time course of SIA if inescapable shock were experienced only in the PVC tubes and the ITI was spent in a very distinct environment? That is, would the shock context then become more aversive? Second, would repeated removal from and return to the shock context serve as a compound CS that would more effectively signal the onset of shock? This manipulation is not unlike the manner in which Siegal manipulates context in a drug injection procedure. In Siegal's studies the ritualistic sequence of events leading up to drug injection (UCS presentation) serves as a danger signal that triggers anticipatory responding. Repeated exposure to the shock context in a ritualistic pattern prior to shock is perhaps analogous to this. In the present experiments this ritual comprised of the repetitive pattern that the rats went through prior to the start of the experiments (removal from the homecage, transport to the lab, being loaded into the tubes, having the tail discs fitted and taped into place). Taken together, this literature and the results of the present study suggest that possibilities for inducing "super analgesia" exist on a scale well in excess of previous estimates. The possibility of "super analgesia" is very intriguing. Although certain technical problems exist, the hypothesis is emminently testable.

The effort required to explore these avenues thoroughly is certainly justified in light of the potential benefits.

Control and maximization of the activity of endogenous pain inhibition systems has promising implications for clinical problems. These implications apply particularly to those situations in which people are exposed to acute noxious stimulation in a patterned manner with a distinct series of events leading up to the noxious stimulation (e.g. burn treatment, physiotherapy, post operative recovery, dental work, labour pains, etc.). The present study has demonstrated that for the rat, at least, forewarned is forearmed. It is now incumbent upon researchers to find techniques for delivering effective signals to the human CNS that enable endogenous pain control systems to function optimally and thereby speed the healing process while improving patient comfort.

In conclusion, it is necessary to reiterate that the present effort has been more successful in generating questions than at answering them. However the obtained results have been very suggestive and specific steps have been outlined that may shed light on the sublties of SIA.

The present study has increased both the magnitude and time course of SIA. SIA at 24 hours actually increased from initial levels. This SIA also lasted longer than has previously been reported. Most important, the time course of SIA was significantly shortened by a change of tail flick test context. An analysis of the theoretical implications of contextual control of SIA has suggested that current concepts concerning the magnitude, time course and etiology

of SIA are in need of more carefully controlled experimentation. In particular, the possibility that the prepotent variable in SIA is similarity of contexts and not controllability has interesting implications for the learned helplessness model.

The major thrust of the present study has been to underline the need for stricter experimental control over a fascinating if not slightly capricious phenomenon. The findings of these future experiments are hard to guess, however, it is likely that subsequent examinations will support the maxim "control conditions and you shall see order".

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Appendix 1: Baseline Source Table

The source table below represents the results of a repeated measures analysis of variance with 2 within subjects factors. Factor A represents trials with 4 levels, Factor B is sessions with 4 levels.

SOURCE	SUMS OF SQUARES	DF	MEAN SQUARE	F	Prob
A	66.803	3	22.268	8.297	.003
ERROR	56.359	21	2.6838		
(epsilon correction=.84498)					
B	78.086	3	26.029	3.463	.053
ERROR	157.82	21	7.5154		
(epsilon correction=.85462)					
AB	32.444	9	3.6049	.8674	.436
ERROR	261.82	63	4.1559		
(epsilon correction=.30394)					

Appendix 2: Experiment 1 Source Table

Summarized below is a 2x2x4x2 mixed analysis of variance. The between groups factors are odor at shock (A, 2 levels) and odor at tail flick test (B, 2 levels). The within subjects factors are trials (C, 4 levels) and sessions (D, 2 levels).

SOURCE	SUMS OF SQUARES	DF	MEAN SQUARE	F	Prob
A	40.696	1	40.696	.8487	.365
B	33.967	1	33.967	.7050	.408
AB	61.632	1	61.632	1.279	.267
Error	1349.0	28	48.179		
C	40.628	3	13.543	1.377	.258
CA	35.082	3	11.964	1.189	.310
CB	128.46	3	42.821	4.355	.016
CAB	5.6509	3	1.8686	.1900	.827
ERROR	826.0	84	9.8344		
(epsilon correction=.8888)					
D	176.11	1	176.11	5.323	.028
DA	6.3347	1	6.3347	.1915	.665
DB	1.9373	1	1.9373	.0585	.810
DAB	8.2692	1	8.2692	.2499	.621
ERROR	926.36	28	33.084		
(epsilon correction=1.0)					
CD	136.11	3	45.371	6.987	.010

CDA	27.8500	3	9.2832	1.430	.237
CDB	77.681	3	25.894	3.988	.051
ERROR	545.53	84			

(epsilon correction=.59784)

Appendix 3: Baseline & Experiment 1 Source Table

This source table is the result of a 5x4x2 mixed analysis of variance. The between groups factor(C) represents the groups variable and has 5 levels. The first within subjects factor is trials(A) which has 4 levels. The second within subjects factor is sessions(B) and has 2 levels.

SOURCE	SUMS OF SQUARES	DF	MEAN SQUARE	F	Prob
C	2767.0	4	691.74	16.45	.0001
ERROR	1471.9	35	42.053		
A	20.365	3	6.7885	.7693	.4662
AC	216.22	12	18.019	2.042	.037
ERROR	926.49	105	8.8237		
(epsilon correction=.90413)					
AB	114.58	3	38.192	6.036	.0168
ABC	153.59	12	12.799	2.023	.0661
ERROR	664.34	105	6.3271		
(epsilon=.59655)					
B	114.58	1	90.153	3.171	.0836
BC	130.69	4	32.673	1.149	.3498
ERROR	664.34	105	6.3271		
(epsilon correction=1.00)					

Appendix 4: Experiment 2 Source Table

This source table is the result of a 4x4x3 mixed analysis of variance. The between groups factor is apparatus types(C) with 4 levels. The first within subjects factor is trials(A) with 4 levels. The second within subjects factor is sessions(B) with 3 levels.

SOURCE	SUMS OF SQUARES	DF	MEAN SQUARE	F	Prob.
C	980.99	3	327.0	3.748	.0221
ERROR	2442.9	28	87.247		
B	172.14	3	57.378	4.649	.0125
CB	138.85	9	15.427	1.250	.2873
ERROR	1036.8	84	12.343		
(epsilon=.86835)					
A	383.21	2	191.60	4.934	.0106
AB	223.10	6	37.183	.9576	.4622
ERROR	2174.6	56	38.831		
(epsilon=.99858)					
CA	33.020	6	5.5034	.4047	.7499
CAB	290.83	18	16.157	1.188	.3079
ERROR	2284.5	168	13.598		
(epsilon=.5975)					

Appendix 5: Experiment 2 Planned Comparisons

This source table is the result of the planned comparisons which were made in experiment 2.

SOURCE	SUMS OF SQUARES	DF	MEAN SQUARE	F	Prob
same vs diff. odor	23.857	1	23.857	.2734	.605
ERROR		28	87.57		
no odor tube vs mesh	360.60	1	36.060	4.133	.051
ERROR		28	87.247		
same & diff. odor vs. no odor & mesh	596.62	1	596.62	6.838	.014
ERROR		28	87.247		

MEANS AND WEIGHTS FOR THE THREE COMPARISNS

	Same Odor	Different Odor	No Odor	Mesh
	13.294	13.999	12.524	9.78
Comp 1	1	-1	0	0
Comp 2	0	0	1	-1
Comp 3	1	1	-1	-1

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